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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,530	06/20/2005	Tatsuo Hoshino	21298 US (C038435/0183236	8399

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EXAMINER	
MARX, IRENE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,530	HOSHINO ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,13-21* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,13 and 15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 6/20/08 is acknowledged.

Claims 2-3, 13, and 15-21 are being considered on the merits to the extent that they pertain to *Xanthophyllomyces* and to the phenoxypropylamine type squalene inhibitor [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine.

Claim 14 is withdrawn from consideration as directed to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 13, and 15-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is confusing in the use of the phrase "a substrate for producing carotenoids including astaxanthin". As written, it appears that the substrate for producing carotenoids includes astaxanthin, which appears inconsistent.

Claim 2 is vague, indefinite and confusing in the recitation of "greater than". When a word of degree is used to modify a limitation, it is necessary to determine whether the specification provides some standard for measuring that degree. See Seattle Box Company, Inc. V. Industrial Crating & Packing, Inc., 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). In this case, the specification does not enable one skilled in the art to reasonably establish what may be construed as being within the metes and bounds of the limitation as modified by the word of degree. Therefore, one of ordinary skill in the art would not be apprised as to the claimed invention's scope when the claims are read in light of the specification. See Ex parte Oetiker, 23 USPQ2d 1641.

Claim 18 is confusing in that applicant fails to set forth the criteria that define a "concentration of the said inhibitor" other than providing a functional definition of "inhibitor" as "giving less than … reduction of the cell growth" of undefined microorganisms using undefined

inhibitors. Also, it is unclear how the concentration correlates with the production of "greater" astaxanthin content as now required. Such functional language describes nothing about the chemical, physical or structural properties of the strain used, the compounds used or their concentration.

Attention is directed to *General Electric Company v. Wabash Appliance Corporation* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed.: "the vice of a functional claim exists not only when a claim is 'wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty".

Functional language at the point of novelty is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outline goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". Claims employing functional language at the point of novelty neither provide those element required to practice the invention, nor "inform the public during the life of the patent of the limits of the monopoly asserted.", *General Electric Co. v. Wabash Appliance Corp.*, at 468.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant argues that one of ordinary skill in the art would know the concentration intended by reading the specification. However, not all of the members of genus *Xanthophyllomyces (Phaffia)* have the same requirements and react the same way to inhibitors. Therefore, the amount required to meet the claim limitations is at least ambiguous and variable depending on the strain cultured and on the culturing conditions therefor.

All the specification provides as "guidance" is:

"In the present invention, the inhibitor for sterol biosynthesis from FPP is added to the medium. Suitably, the concentration of the inhibitor is varied based on the species of inhibitor and microorganism used for the carotenoids production, e.g. in a range of concentration that gives less than 50 % reduction of the cell growth in the carotenoids producing conditions. A

more preferable concentration of the inhibitor may be in the range of concentration that gives less than 30 % reduction of the cell growth"

This is not deemed to be informative as to the specific concentrations required.

As to the example, it pertains specifically to the combination of culturing *Phaffia rhodozyma* ATCC 96594 using the inhibitor [3- (3-allyl-biphenyl-4-yloxy)- propyl]-isopropyl-amine in various specific concentrations. This disclosure pertains to the elected species of inhibitor, but does not pertain to the claims as written which are not so limited.

Therefore the rejection is deemed proper and it is adhered to.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ a specific strain of *Xanthophyllomyces*. It is not clear if the written description is sufficiently repeatable to avoid the need for a deposit. Further it is unclear if the starting materials were readily available to the public at the time of invention.

It appears that a deposit was made in this application as filed as noted on page 3 of the specification. However, it is not clear if the deposit meets all of the criteria set forth in 37 CFR 1.801-1.809. Applicant or applicant's representative may provide assurance of compliance with the requirements of 35 U.S.C § 112, first paragraph, in the following manner.

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection and rejection based on a lack of availability of biological material.

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restriction on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

5. States that the material has been deposited under conditions that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g. see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository and the complete taxonomic description.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant indicates that the strain of claim 3 was redeposited at the ATCC on April 8, 1998. However, the claim pertains to ATCC96594, the old number. The new deposit accession number is not mentioned with any specificity in the Response. Thus it is unclear which deposit

is addressed by applicant's averments at page 11, paragraph 1 of the Response. Moreover, the correct deposit number should be in the claim.

Therefore the rejection is deemed proper and it is adhered to.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-3, 13, and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over An *et al.* taken with Brown *et al.* for the reasons as stated in the last Office action and the further reasons below.

The claims are directed to a method of culturing a *Xanthophyllomyces(Phaffia)* that is capable of producing carotenoids including astaxanthin in the presence of an inhibitor of squalene synthase inhibitor and wherein the astaxanthin content is greater than without the inhibitor.

An *et al.* discloses a method of culturing strains of *Xanthophyllomyces(Phaffia)* that is capable of producing carotenoids in the presence of an inhibitor of squalene synthase. See, e.g., page 118, paragraph 2. Although the reference reports that the method of culturing in the presence of an inhibitor of sterol synthesis did not appear to have greater astaxanthin content, this was not, in fact, measured with any precision, but rather only eye-balled. Therefore one of ordinary skill in the art would reasonably have expected some increase even though it might not be readily apparent to the naked eye..

The reference differs from the claimed invention in that the inhibitor of squalene synthase is not a phenoxypropylamine compound and is not specifically [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine. However, Brown *et al.* adequately demonstrate that this phenoxypropylamine compound is known in the art as a squalene synthase inhibitor.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of An *et al.* by culturing *Xanthophyllomyces(Phaffia)* for the production of a variety of carotenoids including astaxanthin using a different inhibitor of squalene synthase inhibitor such as the phenoxypropylamine compound [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine for the expected benefit of maximizing the yield of the valuable compounds carotenoids including astaxanthin useful as food additives and in pharmaceutical applications.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant(s) argue(s) that there is no suggestion to combine references. However, motivation can come not only from direct teaching of the prior art, but also the nature of the problem to be solved and/or the knowledge of persons of ordinary skill in the art, Ruiz v. A.B. Chance Co. 357 F.3d 1270, 69 USPQ2d 1686 (2004). The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966). Further, the examiner recognizes that references cannot be arbitrarily combined that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references, *In re* Nomiya, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. One test for combining references is what the combination of dislosures taken as a whole would suggest to one versed in the art, rather than by their specific disclosures, *In re* Bozek, 163 USPQ 545 (CCPA 1969). In this case, the combination of An *et al.* which teaches the use of inhibitors of sterol biosynthesis in the production of carotenoids with

Xanthophyllomyces(Phaffia) , and Brown which teaches that the specific compound exemplified and selected is known in the art for the desired effect in inhibiting sterol biosynthesis, is considered to be obvious in the absence of evidence to the contrary.

Note still further that, contrary to applicant's argument, it is well established that motivation for combining references need not come from the references themselves, as long as applicant's disclosure is not improperly used in a hindsight reconstruction of the claimed invention. *See Ex parte Levengood*, 28 USPQ2d 1300 (1993), at 1301. ("Motivation for combining the references need not be explicitly found in the references themselves. Indeed, the examiner may provide an explanation based on logic and sound scientific reasoning that will support a holding of obviousness.")(Citations omitted.)

Applicant's negative interpretation of the An *et al.* paper regarding astaxanthin production is noted. However, the claims are directed to the production of "carotenoids including astaxanthin" and all the proviso requires if "greater" astaxanthin content than in the absence of inhibitor without an indication of the amount of increase required. It is noted in this regard that the reference pertains to "resistance" to sterol inhibitors after mutation events for selection purposes wherein certain concentrations are used, while the present claims are directed to cultivation in the "presence" of an unknown quantity of an unknown inhibitor having a certain function. In addition, the extent of "greater" astaxanthin content in the present claims is not defined with any particularity. Therefore, the amount of the increase intended cannot be determined with any precision and encompasses even a tiny increase which may not be readily detectable with the naked eye.

Applicant argues that there would be no expectation of success upon reading the disclosure of An *et al.*. Yet, as noted above, the reference pertains to selection of mutants that produce carotenoids and which demonstrate "resistance" to inhibitors, while the invention as claimed is directed to the "presence" of an inhibitor or to the "presence" a specific inhibitor. Thus, the concentration of inhibitor used cannot be readily determined. The reference clearly suggests that sterol biosynthesis inhibitors are expected to be involved in increases of carotenoid production including astaxanthin.

In addition, the results of Table 2 of the as-filed specification show that at day 4 of cultivation the results are better without addition of the specific squalene synthase inhibitor [3-

(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine than with the addition of 5 μg/ml even for the specific strain ATCC 96584 in a specific medium. Thus, it is apparent that the length of cultivation as well as the concentration of the specific inhibitor [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine affect the astaxanthin content obtained for a specific high producing strain such as *Xanthophyllomyces(Phaffia)* ATCC 96584. Yet only in dependent claim 3 is this specific strain of *Xanthophyllomyces(Phaffia)* cultured. Thus, the results presented in the specification cannot be readily extrapolated to the broad invention as claimed, since the results obtained suggest to one of ordinary skill in the art that the effects on carotenoid and astaxanthin production are dependent on the strain of *Xanthophyllomyces(Phaffia)* cultured as well as the type and concentration of inhibitor used in the culturing process.

The claims are not commensurate in scope with the arguments or the results in the specification. The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim.

Therefore the rejection is deemed proper and it is adhered to.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Irene Marx/
Primary Examiner
Art Unit 1651